PALL Pall Corporation

25 Harbor Park Drive
Port Washington, NY 11050 USA

516.484.3600 phone
516 484.3628 fax
www.pall.com

September 9, 2004

Division of Dockets Management
5630 Fishers Lane, room 1061
Rockville, Maryland 20852

Re: Food and Drug Administration, HHS
Center for Food Safety and Applied Nutrition
Docket No. 2004N-0230

Dear Reviewer:

This submission is in response to the request for scientific information about the current state of quality management techniques, quality systems approaches and industry practices concerning controls used by food manufacturers and processors to prevent food borne hazards. This submission also responds to the specific questions posed by FDA to address potential hazards in the food supply.

As a major long-time supplier of filtration, purification and separation equipment for the removal of contaminants in food and beverage applications, Pall Corporation concurs with the need to modernize the Current Good Manufacturing Practice (CGMP) regulations for food to reflect the new contamination control technology, industry practices and quality assurance techniques introduced during the past two decades.

In particular, the development and widespread use of biocompatible, positively-charged and uncharged membrane filters (produced by several manufacturers), innovative shear-driven separation equipment, and automated control systems for their operation, has resulted in filter products which are used at critical control points to reliably maintain defined bioburden limits or acceptable sterility assurance levels of all types of fluids while increasing overall product yields and retaining taste characteristics. The benefits and desirability of eliminating physical, chemical and microbiological hazards through the use of filtration systems also include the ability to nondestructively and non-invasively test the integrity of these systems, thereby providing documented evidence of their ongoing functionality and efficacy while in service.

In connection with this submittal, as well as to provide a forum for the exchange of scientific and educational information, Pall will be pleased to present at your convenience a seminar and/or roundtable discussion on filtration technology and its current applications in food and beverage processes as part of an HACCP or quality systems approach. We have previously made such noncommercial presentations for FDA personnel at the Center for Drug Evaluation & Research, the Center for Biologics Evaluation & Research, various district offices and FDA workshops, where the focus was on aseptic processing, fermentation and other filtration technology applications in the pharmaceutical industry.

Specific Comments
While the control of physical, chemical and microbiological hazards is understandably the primary agency focus in order to protect the public health, there is also a need to address the removal of "undesirable microorganisms" (as defined in 21CFR110.3(i)) although they may pose little, if any, public health risk. The presence of these microbes may nevertheless pose a danger to certain segments of the population who cannot tolerate them, their residues or the food decomposition they cause. Undesirable microorganisms also require periodic review with respect to emerging pathogens.

Undesirable microorganisms may also pose an economic risk to the manufacturer. Potential economic risks may result, for example, from alterations in product taste, consistency or appearance. Economic risk can also encompass product liability concerns, product recalls or manufacturing inefficiencies. These considerable risks can be prevented by implementing appropriate process control systems (e.g. use of bacterially retentive filters whose performance is validated with non-destructive integrity tests), and product quality tests performed in-process or during filling of the final product.

Therefore, we urge that the following three provisions be added to the appropriate sections of FDA's CGMP in manufacturing, packing, or holding human food regulations.

110.20(b)(8). Air filtration systems, including prefilters and particulate matter air filters, shall be used when appropriate on air supplies to production areas and on tank vents holding a food product or ingredient. If air is recirculated to production areas, measures shall be taken to control recirculation of dust from production. In areas where air contamination occurs during production, there shall be adequate exhaust systems or other systems adequate to control contaminants.

110.40(h). Filters and separation systems for liquids shall be provided when appropriate for adequate control over microorganisms, particulates and other hazardous or undesirable physical, chemical or microbiological contaminants. As close as possible prior to actual use, the integrity of bacterially retentive final filters used at critical control points shall be verified through routine testing by a pressure hold test or a diffusive air forward flow test.

110.80(b)(4). Measures such as filtration shall be used to physically remove hazardous or undesirable microorganisms when appropriate.

General Comments

Our comments and information which follow are arranged to correspond to the three potential hazards and the eleven questions contained in your Federal Register notice. Hazards described below may be intrinsic or extrinsic to the processing environment. Extrinsic hazards include those introduced accidentally through human error or by inadequate process controls, as well as those introduced deliberately by disgruntled workers, terrorists or untrained operators.

Questions

In general, how should the CGMP regulations in part 110 be revised or otherwise modernized? Please describe, generally, the shortcomings of the current regulations.

While part 110 has long served to protect the public health, the introduction of new processing technologies and controls for the safe production of food can further lower risks and enhance manufacturers' economics. Therefore, part 110 should be modernized to explicitly recognize new processing technologies and controls, as well as address shortcomings of the current regulations in the following areas:

1. Water quality used throughout food manufacturing plants should be subjected to a risk analysis, and criteria established for water for cleaning or initial rinsing, water for product contact or final rinsing, and water for manufacture. Guidelines for water systems, based on HACCP analysis and economic factors, should be issued.

2. A culture promoting product quality and a quality system (e.g. ISO9001:2000) should be emphasized by elevating the section on Personnel in the General Provisions of part 110 to form the basis of a separate subpart addressing Organization and Personnel. This subpart would include employee training and the responsibilities of the quality control unit to perform documented qualification or validation testing of critical processes.

3. Compressed air or gas used throughout food manufacturing plants, as well as ambient air, should be subjected to a risk analysis, and criteria established for air in

controlled environment areas, air over filling lines and compressed air or gas in contact with food. Guidelines for air quality, based on HACCP analysis and economic factors, should be issued.

4. Elaboration regarding pasteurization, including broadening to list other microbial removal or destructive treatments, should be addressed in 21CFR110.80 (2) by adding definitions which encompass current acceptable technologies, and enumerating the steps required to qualify new technologies for microbial removal or destruction. Physical removal of microorganisms should be explicitly included in 21CFR 110.80 b(2) and 21CFR 110.80 b(4) in order to avoid inadvertently limiting the available, validated technologies manufacturers would otherwise consider.

5. Supplier certifications for raw materials and equipment used in critical operations should be encouraged. Guidelines for review of such documentation and for in-house test programs may be needed to help ensure supplier compliance with the unique needs of food and beverage manufacturers.

6. Security issues should be explicitly addressed in the modernized CGMP regulations, including the following.

- o Elucidation of personnel security requirements, including guidelines for background checks and interaction with external security agencies (police, Interpol, FBI, Homeland Security) should be listed.
- o Plant and property security issues should be addressed, such as mention of tamper-proof security on bulk chemical vessels, water supplies, chemical dosing and physical barriers. Minimum ventilation (scfm or m3/minute) guidelines for both normal operation and emergency use should be issued for a variety of representative processes and facility capacities (e.g. number of workers).
- o Production and process control security system guidelines should be issued, including the use of control panel lock-out devices and password protection features.
- o Definition of a closed or safe system should be added to 21CFR 110.3. This definition should include illustrative examples, such as fermentation tanks or transport tanker trucks which are vented directly to the atmosphere being examples of open systems whereas installation of vent filters rated for complete bacterial retention would transform these to closed systems. In fact, in Great Britain, filters are recommended on tanker trucks containing milk and passing through or from areas infected by the foot and mouth disease virus (FMDV), in order to reduce the risk of spread to uninfected areas.

1. Which practices specified in current part 110 are most effective at preventing each type of food hazard? Which practices are least effective at such prevention?

Physical hazards include particulates coming from packaging (e.g. glass or plastic from bottles), raw materials, processing or treatment agents, processing equipment, pests and dirt.

There are a variety of measures that successfully control particulate contamination in specific processing environments. While successful application in the wide variety of food and beverage production facilities is a challenge, in general, the following measures apply to the majority of production facilities:

- Proper design and facility maintenance (e.g. positive air flow systems)
- Mechanical separation practices (e.g. sieves, traps, metal detectors)
- Washing of raw materials to remove physical contamination
- Inspection of raw materials and food ingredients
- Use of compressed air (free from particulates, oil and oil vapor) to clean surfaces or blow out containers
- Use of filling line filters or other filtration equipment for final products, in-process products, incoming plant water, and waste water, applying a filter that has fixed media, a removal rating yielding greater than 99.998% removal of particles at a specific micron size (to be determined by specific need at that processing step), and is compatible with chemicals, adjuvants and production aids used in the processing line, as well as the food product itself.

The goal of these processing steps or controls is to remove particulate matter without adversely affecting the qualitative and quantitative food product characteristics. Associated measurements may include the use of mechanized optical control or visual inspection systems for containers (only for optically clear products), as well as equipment for measuring particle size distribution at specific points in the process line.

There are a variety of processes which taken in isolation do not effectively prevent particulate hazards; these include centrifugation, flotation, loose media filtration, irradiation, and visual inspection for opaque products. However, when these processes are taken in combination with the technologies and control steps listed above, then they can provide a product with a greater degree of assurance of safety.

The economic impact of using multiple technologies *versus* a single technology for any specific processing step should be reviewed by the food producer and suppliers. This decision will have implications on the economics of all downstream processing steps and potentially may reduce or increase process flexibility as well as increase or decrease downstream costs. Such a review should be based on life cycle costing to accurately reflect the economic impact.

A preferred approach would have food and beverage producers utilize a HACCP plan to first evaluate specific risks that may pose public health problems. Following this review producers should look at the process as a whole to determine where their economic risks may be.

Chemical hazards include substances coming from raw materials and process treatment agents (e.g. for cleaning, for specific reactions), and may also be released from microbes introduced into the process.

Adsorption and filtration technologies are the most effective at removing chemical substances introduced intentionally or accidentally into a process. Specific technologies include adsorbers like PAC/GAC (powdered and granular activated carbon), ion exchange resins and adsorptive filters. For example, for many beverage products chlorine must be removed from incoming plant water and wash water so as not to negatively impact the final product taste. Economic hazards may be removed during processing with agents such as bentonite, gelatine or PVPP (polyvinylpolypyrrolidone). Filtration processes like ultrafiltration, nanofiltration and reverse osmosis may also be used to remove chemical agents. Additionally, the use of validated equipment cleaning procedures will control chemical residues and reduce the risk of contamination in the final product.

Microbiological hazards are varied but fall into the following categories:

- Organisms that are introduced into the process as part of a raw material or during processing
- Organisms that are common contaminants from the environment (air, water, soil, personnel)
- Organisms that could be deliberately added to the process or final product.

Many microbes pose more of an economic risk to the food and beverage producer than a direct risk to public health and consumers. Regardless of type of risk, microfiltration removes or reduces microbial contamination (i.e. yeast, bacteria, protozoans, and viruses). The advantages of removing microbes instead of killing them within the product (e.g. by pasteurization, UV or ozone sanitization) include reducing the risk of bacterial spores germinating in the final product, removing the source of heat stable toxins (present in some pathogenic bacteria), and removing microbial contents (lipopolysaccharide/endotoxins, nucleic acids, and enzymes).

Irrespective of the nature of the organism (pathogenic, opportunistic pathogen, economic risk, noneconomic risk), or the method of introduction, filtration can remove this type of contamination.

Filtration can be implemented at various stages during a production process and is applied to achieve a defined level of microbial removal using qualified or validated procedures. The broad array of products manufactured requires each manufacturer to determine the appropriate processing level to control microbial status. For example, highly viscous fluids like high fructose corn syrup (HFCS) are intrinsically microbially stable. There may be microbes detected in the HFCS, but these organisms do not grow in the product due to osmotic pressure and other factors. Due to the product characteristics it is often difficult and may be economically challenging to remove or reduce the number of these static microorganisms in HFCS. On the other hand, HFCS is usually used as a raw material for other producers. When diluted, these static organisms (often molds and yeast) will proliferate in low acid beverage products. Producers of low acid beverage products, therefore, employ additional processing steps like filtration to reduce or completely remove microbes. Thus, HFCS producers may focus on removal of visible particulates that requires different filtration technology than beverage producers that employ membrane media.

Filters used for microbial removal are made of fixed/stable membranes or other media. Final filters used prior to product packaging should undergo an integrity test that can be readily performed by the manufacturer, and which is validated by correlation with microbial removal data.

Microorganism type	**Removal Rating**	**Comments**
Protozoan (e.g. *Giardia* and *Cryptosporidium*)	1 micron	Validation is sometimes performed with latex bead challenges due to safety risk of working with this class of organisms. Validation may also be performed with killed or live organisms.
Yeast and molds (*e.g. Saccharomyces*)	0.65 micron	Most vegetative yeast are removed efficiently with a 0.65 micron membrane filter. However, some yeast in stationary phase or early lag phase may penetrate 0.65 micron membrane filters. As these yeast do not pose health risks but only economic risk we recommend reducing the filter rating to 0.45 micron if this condition exists.

Spore forming bacteria (*e.g. Bacillus* species)	0.45 micron	Bacterial spores have been shown to be removed by 0.45 micron membrane filters.
Coliform bacteria and bacteria with heat-stable toxin virulence factors (*e.g. Escherichia coli, Serratia, Shigella, Salmonella, Campylobacter*)	0.45 micron	Microbial challenge data available for specific organisms or model organisms demonstrating complete removal or providing a titer reduction.
Bacteria used in or contaminating fermentation processes (*e.g. Oenococcus oeni, Pediococcus, Lactobacillus, Legionella*)	0.45 micron	Microbial challenge data available for validated filters demonstrating removal or reduction of common contaminants.
Waterborne bacteria (*e.g. Pseudomonas* species)	0.2 micron	Microbial challenge data available for validated filters demonstrating removal or reduction of common contaminants.
Virus in liquid products (*e.g. Caliciviridae*, Poliovirus, Adenovirus, Coxsackie virus, Echovirus)	Ultra or Nano filtration; 20 nm and 50 nm membranes	Specific microbial challenge tests are not yet generally available. This is partially due to virus detection problems including inability to culture and difficulties with laboratory contamination (nucleic acid based technologies).
Virus in gas products or vents (*e.g.* bacteriophages, aerosolized viruses from plant personnel)	0.2 micron hydrophobic medium	Microbial challenge data available for validated filters demonstrating removal or reduction of common contaminants.

For products that cannot be filtered, like raw fruits, vegetables, meats and poultry, microbial risk may be limited by filtering product wash water, thus removing potential contaminants. Microbes may be introduced from the environment during process storage steps. Introduction of bacteriophages into cheese fermentation, for example, can cause reduction in product yields. For storage tanks and fermentation vessels, Pall strongly recommend installation of sterilizing grade gas or vent filters. These

hydrophobic filters should have validated integrity test values correlated to removal of specific microbes in both air and liquid service (since liquid service represents a worst case scenario for vent filters which may inadvertently become wet).

2. In today's food manufacturing environment, what conditions, practices, or other factors are the principal contributors to each type of food hazard?

Physical hazards may be present due to a variety of processing events including: glass particles due to breaks during bottle rinsing; incomplete processing (e.g. sedimentation); incomplete incoming raw material inspection or processing; no filtration for steam, gas/air, or storage tank vents; and metal from processing equipment.

Chemical hazards are often caused by misapplication of chemicals used for cleaning or processing. This may be caused by problems with equipment design, limited employee training or lack of specific process protocols. Additional economic hazards may include lack of process control, for example, exposure to oxygen may cause products to oxidize and have a reduction in qualitative and quantitative flavor.

The principal contributors of microbial hazards include water used in the product or for cleaning, air/gas, and organisms introduced by plant personnel.

3. If the CGMP regulations were revised, which type or types of food hazards could be most readily prevented through CGMP-type controls?

All physical, chemical and microbial food hazards could be readily prevented through CGMP-type controls. This is confirmed by extensive experience with aseptic processes.

4. Are there preventive controls, in addition to those set out in part 110, needed to reduce, control, or eliminate each of the three types of food hazards? If yes, please identify the specific hazard and the particular controls, that would reduce, control, or eliminate the hazard.

Yes, additional preventive controls other than those currently set out in part 110 are needed to reduce, control or eliminate food hazards.

Controls and measurements are often specific to market segments. For example, the measurement of turbidity and colloids aids wine producers in the economic control of their systems. These measurements are not important for dairy manufacturers who may find more use for installation of metal detectors and magnets to remove particulate hazards.

Chemical hazards may be reduced by introducing specific product characteristic measurements (e.g. conductivity, pH, proteins, polyphenols, iron cations, oxygen levels, temperature, total organic carbon, etc.) and setting specifications as well as monitoring product samples.

Controlling microbiological hazards may also include in-process or raw materials monitoring. Now there are many rapid microbiological technologies available that allow food and beverage manufacturers to generate information regarding typical bioburden levels. This information may be important for identifying possible deviations from normal conditions that may impact the efficiency of downstream technologies. However, if downstream processes are selected to remove or reduce microorganisms regardless of the incoming load, then these measurements provide no additional health risk reduction benefit. Thus, application of rapid microbiological detection could be applied in-process for economic reasons, but should be applied to finished product in order to meet regulatory requirements for health and safety assurance.

5. What concepts or underlying principles should guide FDA's adoption of new preventive controls?

The ability to validate safety and efficacy should guide the adoption of new preventive controls. If validation data is available from a supplier or food product manufacturer, then adoption of these validated new preventive controls will help ensure the safety of foods. Validated preventive controls are useful at the source, during processing and/or throughout the packaging, handling and distribution process. Application of these controls should be part of a quality program that includes internal and external auditing, operator training, control of raw materials, periodic check of production equipment, product and raw material traceability. ISO9001:2000 combined with HACCP concepts should constitute the core of this quality program in order to aid producers in meeting CGMP requirements.

6. How should the effectiveness of preventive controls for each of the three types of hazards be most accurately measured?

Validated controls require minimal periodic monitoring to verify their continuing effectiveness. For example, validated filters merely require an integrity test to verify their removal rating. In general, the effectiveness of preventive controls can be most accurately measured by control charts, narrow limit gauging and other well-established quality control techniques. Records of out of specification incidents should be maintained by manufacturers, and the reduction or elimination of these incidents would demonstrate the effectiveness of the specific controls that were implemented.

7. In today's food manufacturing environment, what are the principal contributors to the presence of undeclared allergens in food? For example, do labeling errors or cross-contamination contribute? Which preventive controls could help reduce, control, or eliminate the presence of undeclared allergens in food?

The presence of allergens is often due to inadequate raw material labeling and traceability of materials within a production plant. This topic is outside our scope of expertise.

8. Are there existing quality systems or standards (such as international standards) that FDA should consider as part of the agency's exploration of food CGMP modernization? Please identify these systems or standards and explain what their consideration might contribute to this effort.

FDA should consider the following international standards:

- The ISO quality system directs manufacturers to apply controls and measurements, define responsibility, and handle out of specification performance events. Handling these issues are essential for compliance with CGMP.
- IFS (International Food Standard) sets standards for European producers. As many companies are global in nature, consolidation or harmonization of requirements will aid compliance and encourage import and export of food products.
- BRC (British Retail Consortium) publishes a specific global standard for food. This standard allows external audits of a manufacturing location and standardizes food safety criteria and monitoring procedures.
- Trade association standards including IDF (International Dairy Foundation), IBWA (International Bottled Water Association), NSDA (National Soft Drink Association), ISBT (International Society of Beverage Technologists) and many others, are written by expert members of technical committees. These technical committees review new product processing issues as well as compliance with government regulations. Additionally, some of these trade associations have quite stringent production requirements that FDA should consider.
- Codex Alimentarius is a subset of the FAO/WHO food standards program. As the main goal of this program is to protect consumer health, it should correspond well with the FDA's own goals to protect the public health and safety. Additionally, this program promotes the coordination of all food standards work internationally.

9. There is a broad variation within the food manufacturing and processing industry, including variations in size of establishments, the nature of the food produced, the degree to which the food is processed, and the vulnerability of a particular operation to physical, chemical, or microbial hazards. How, if at all, should the CGMP regulations be revised to take into account such variation? For example, should there be different sets of preventive controls for identifiable segments of the food industry, such as different storage temperature limits?

While there is broad variation within the food manufacturing and processing industry, there is also broad applicability of well-established quality control principles. Moreover, the FDA has considerable experience in the application of parametric standards. As a result, by focusing on what controls to apply, rather than how to apply them, the FDA can successfully modernize the CGMP regulations to create a single set of minimum requirements for preventive controls for the entire industry. Variation within the industry can then be better addressed by issuing separate guidelines which delineate specific supplemental preventive controls for particular segments of the food industry.

10. There are a number of measures, procedures, and programs that help to ensure that preventive controls are carried out adequately. These include the following items: training programs for managers and/or workers; audit programs; written records, *e.g.*, batch records, sanitation records; validation of control measures; written sanitation standard operating procedures; food label review and control program; and testing of incoming raw materials, in process materials, or finished products. Which (if any) of these should be required practices for food and manufacturers and why? Which (if any) of these should be recommended practices for food manufacturers and processors and why?

Training programs and validation of control measures should be required practices because they are oriented to ensuring product fitness for use, thereby reducing public health risks as well as preventing economic loss. By focusing on process adequacy and process control, they prevent hazards and foster planning.

In contrast, written records and inspection programs are oriented toward detection and conformance to specifications. These should be recommended practices, but not required because they are a less effective means to an end. Preventing hazards is preferable to removing them if detected.

In addition, validating process adequacy and implementing effective training programs are relatively lengthy processes which can take years to develop properly, whereas documentation and inspection procedures can be implemented relatively quickly as needed. While both required and recommended practices have their place in a quality management system, the difference in emphasis would allow manufacturers and processors greater flexibility to meet CGMP requirements within their market segments without impairing safety.

11. Are there preventive controls in addition to those already set out in part 110 for food distributors, wholesalers, and warehousers that are needed to help ensure the safe and sanitary holding of food? If yes, please identify the controls by hazard and sector of the industry.

This topic is outside our scope of expertise.

Summary Table:

	Physical Hazards	Chemical Hazards	Microbiological Hazards
Which CGMP practices are most effective at preventing each type of food hazard?	Filtration	Adsorptive technology	Filtration with validated filters and integrity tests correlated to microbial removal
Which CGMP practices are least effective at such	Optical inspection for	Centrifugation	UV, pulsed electric fields, centrifuge

prevention?	opaque products; Centrifugation		(bactofugation)
What conditions, practices, or other factors are the principal contributors to each type of food hazard?	Raw ingredients, process water, air/gas supplies and personnel	Raw ingredients, process water, air/gas supplies and personnel	Raw ingredients, process water, air/gas supplies and personnel
Which type or types of food hazards could be most readily prevented through CGMP-type controls?	All hazards including glass, plastic, stones and metal particulates from incoming raw materials or introduced during production	Those chemical hazards originating in service fluids; agrochemicals in water, heavy metals in water, detergents from water, fumigants from air	All microbiological hazards coming from the environment (air and water) and raw materials as well as those introduced by personnel, e.g. bacteria, molds, yeasts, bacteriophages and animal viruses
Identify particular preventive controls (other than CGMP) to reduce, control, or eliminate each of the three types of food hazards.	Validated particulate removal filters and other physical barriers specific to various market segments	Validated adsorptive filters, ionic exchange resins, as well as ultrafiltration and reverse osmosis membranes appropriate for specific chemical contaminants	Validated microbially retentive filters, and use of rapid microbiological assay equipment
What quality concepts or underlying principles should guide FDA's adoption of new preventive controls?	Validation of process adequacy and process controls will	Validation of process adequacy and process controls will ensure	Validation of process adequacy and process controls will ensure product fitness for use by preventing hazards

	ensure product fitness for use by preventing hazards and encouraging quality planning	product fitness for use by preventing hazards and encouraging quality planning	and encouraging quality planning
How should the effectiveness of preventive controls for each of the three types of hazards be most accurately measured?	Periodic monitoring of validated controls (e.g. filter integrity tests) will verify their ongoing effectiveness; Control charts, narrow limit gauging results, and other records showing reduction or elimination of out of specification incidents also verify effectiveness	Periodic monitoring of validated controls (e.g. filter integrity tests) will verify their ongoing effectiveness;C ontrol charts, narrow limit gauging results, and other records showing reduction or elimination of out of specification incidents also verify effectiveness	Periodic monitoring of validated controls (e.g. filter integrity tests) will verify their ongoing effectiveness; Control charts, narrow limit gauging results, and other records showing reduction or elimination of out of specification incidents also verify effectiveness
What are the principal contributors to the presence of undeclared allergens in food? For example, do labeling errors or cross-contamination contribute? Which preventive controls could help reduce, control, or eliminate the presence of undeclared allergens in food?	Outside scope of expertise	Outside scope of expertise	Outside scope of expertise
Are there existing quality	Codex	Codex	Codex Alimentarius,

systems or international standards that FDA should consider? Explain what their consideration might contribute to preventing food hazards.	Alimentarius, ISO, IFS, BRC, and expert technical committees of various trade associations should be considered because harmonization of requirements will aid global compliance and encourage export of food products	Alimentarius, ISO, IFS, BRC, and expert technical committees of various trade associations should be considered because harmonization of requirements will aid global compliance and encourage export of food products	ISO, IFS, BRC, and expert technical committees of various trade associations should be considered because harmonization of requirements will aid global compliance and encourage export of food products
How, if at all, should the CGMP regulations be revised to take into account the broad variation within the food manufacturing and processing industry, including variations in size of establishments, the nature of the food produced, the degree to which the food is processed, and the vulnerability of a particular operation to physical, chemical, or microbial hazards? Should there be different sets of preventive controls for identifiable segments of the food industry, such as different storage temperature limits?	By using a parametric approach and focusing on what controls to apply, rather than how to apply them, the FDA can successfully modernize the CGMP regulations to create a single set of minimum requirements for preventive controls for the entire industry. Variation	By using a parametric approach and focusing on what controls to apply, rather than how to apply them, the FDA can successfully modernize the CGMP regulations to create a single set of minimum requirements for preventive controls for the entire industry. Variation within the industry can then be better addressed by	By using a parametric approach and focusing on what controls to apply, rather than how to apply them, the FDA can successfully modernize the CGMP regulations to create a single set of minimum requirements for preventive controls for the entire industry. Variation within the industry can then be better addressed by issuing separate guidelines which delineate specific supplemental preventive controls for particular segments of the food industry

	Variation within the industry can then be better addressed by issuing separate guidelines which delineate specific supplemental preventive controls for particular segments of the food industry	issuing separate guidelines which delineate specific supplemental preventive controls for particular segments of the food industry	
Which of the following measures, procedures and programs, to ensure that preventive controls are carried out adequately, should be required practices for food manufacturers and why? (see list in text)	Validation of process adequacy, training programs and other preventive controls should be required	Validation of process adequacy, training programs and other preventive controls should be required	Validation of process adequacy, training programs and other preventive controls should be required
Please identify, by industry sector, any additional preventive controls for food distributors, wholesalers, and warehousers that are needed to help ensure the safe and sanitary holding of food.	Environmental controls; particulate generation by pumps	Validation of cleaning processes to prevent cross contamination; removal of decomposition by-products	Air filters for use on milk tankers to prevent possible spread of FMDV (food and mouth disease virus) and other microbiological hazards. Guidelines for water and gas/air quality should establish criteria for the use of

			control measures such as filtration for water for cleaning or initial rinsing, water for product contact or final rinsing, water for manufacture, air in controlled environment areas, air over filling lines and compressed air or gas in contact with food

We appreciate your consideration of the points made above. If there is any additional information that we may be able to provide, then we would be pleased to supply it through meetings, seminars and telephone conversations between FDA staff and Pall scientific personnel. Further information on Pall Corporation is available at www.pall.com. We look forward to continued dialogue with you on this important subject.

Respectfully submitted,
Pall Corporation

Hyman Katz, Ph.D.
Vice President, Quality Assurance
and Regulatory Affairs
Services Department

Lisa M. Madsen, Ph.D.
Principal Scientist
Scientific & Laboratory

Fellow of the American Society for Quality

HK:gd

Enclosures (Literature and Reference Materials)

1. John D. Brantley and Jerry M. Martin, 1997, Integrity Testing of Sterilizing Grade Filters, Pall Publication PBB-STR-28
2. Atsushi Sakuraoka and Lisa M. Madsen, 2001, Removal of Heat-Resistant Bacterial Spores by Filters: Implications for Filter Use in Soft Drink Production, Pall Publication FB-JUICE
3. Atsushi Sakuraoka, Masaru Komaki, Ryoko Ohkubo, Toshiki Yamaguchi and Ibuki Hayasaka, 2002, Removal of Heat Resistant Bacterial Spores Suspended in Syrups and Soft Drinks by Means of a Filter, *Bokin Bobai*, Vol. 30, No. 4, pp. 207-215, The Society for Antibacterial and Antifungal Agents, Japan, Winner of the 2003 Technology Encouragement Prize of the Japan Canners Association
4. L.E. Pearce, 2002, Bacterial diseases - the impact of milk processing to reduce risks, *Bulletin of the International Dairy Federation*, Vol. 372, pp. 20-25
5. U. Hulsen, 1999, Alternative methods to heat treatment, *Deutsche Milchwirtschaft*, Vol. 50, No. 18, pp. 774-779
6. Pall SeitzSchenk, 2002, Technology to Support the Food & Beverage Industry, Pall Publication FB 698a
7. Timothy O'Sullivan, 1992, High Quality Utilities in the Food and Beverage Industry, *Dairy, Food and Environmental Sanitation*, Vol. 12, No. 4, pp. 216-219
8. Pall, 1998, PallSep PS10 Membrane System, Pall Publication F4
9. Pall, 1998, OenoFlow Wine Clarification System, Pall Publication F-5
10. Pall, 1998, OenoClear W Grade Filter Cartridges, Pall Publication E52
11. R. Gaub, S. Lustig and T. Treetzen, 1999, Test results obtained with PFS-filter in fine filtration of beer, *Brauwelt International*, Vol. 139, No. 3, pp. 209-211
12. C.G. Kilner, 2001, letter concerning The Foot and Mouth Disease Order 1983. Air Filters for Use on Milk Tankers, Ministry of Agriculture, Fisheries and Food, UK